"3'-end of an mRNA" includes primarily noncoding sequences (90%-100% of the 3' end is untranslated or noncoding sequence), and thus includes only a relatively short portion that is translated, or is part of a coding region." (Emphasis added)

Support for the addition of the limitation "from 10 nucleotides" to claim 1 is found in the specification at p. 13, lines 15-22, wherein the specification states, [i]n another embodiment, a nucleic acid member comprises a sequence at the 3'-end of an RNA transcript and which is less than 50% of the length of the full length transcript. In one embodiment, the nucleic acid member is any of: 595 nucleotides, 590 nucleotides, 550 nucleotides, 500 nucleotides, 450 nucleotides, 400 nucleotides, 350 nucleotides, 300 nucleotides, 250 nucleotides, 200 nucleotides, 150 nucleotides, 100 nucleotides, 50 nucleotides, 20 nucleotides, 15 nucleotides, **10 nucleotides**, and 8 nucleotides." (Emphasis added)

Claim 2 has been amended to claim "an array comprising a plurality of nucleic acid members, each member having a unique position and stably associated with a solid substrate, wherein each nucleic acid member comprises a sequence of nucleotides corresponding to a non-coding region of a 5' end of an mRNA transcript, and wherein each of said nucleic acid members is from 10 nucleotides to less than 1000 nucleotides."

Support for the amendments to claim 2 are found in the specification at p.9, line 25-p.10, line 2, wherein the specification states, "[a]s used herein, "5'-end of an RNA transcript" refers to at least 8 and less than 1000 contiguous nucleotides of the end of a full length mRNA that includes and is adjacent to the most 5' nucleotide of a full length mRNA, and extends toward the 3'-end of the mRNA (e.g., toward the polyA tail). The "5'-end of an RNA transcript" includes 5' untranslated sequences and may or may not contain coding sequence from the 5' portion of the coding region of a **mRNA**. Preferably, the "5'-end of an RNA transcript" includes primarily noncoding sequences (90%-100% of the 5' end is untranslated or noncoding sequence), and thus includes only a relatively short portion that is translated, or is part of a coding region." (Emphasis added)

Support for the addition of the limitation "from 10 nucleotides" to claim 2 is found in the

specification at p. 13, lines 15-22, wherein the specification states, "[i]n one embodiment of the invention, a nucleic acid member comprises a sequence at the 5'-end of an RNA transcript and which is less than 50% of the length of the full length transcript. In one embodiment, the nucleic acid member is any of: 950 nucleotides, 900 nucleotides, 890 nucleotides, 850 nucleotides, 800 nucleotides, 750 nucleotides, 700 nucleotides, 650 nucleotides, 600 nucleotides, 590 nucleotides, 550 nucleotides, 500 nucleotides, 450 nucleotides, 400 nucleotides, 350 nucleotides, 300 nucleotides, 250 nucleotides, 200 nucleotides, 150 nucleotides, 100 nucleotides, 50 nucleotides, 20 nucleotides, 15 nucleotides, **10 nucleotides**, or 8 nucleotides in length." (Emphasis added)

Support for the inclusion of the phrase "nucleotides corresponding to a non-coding region of a 3' [or 5'] end of an mRNA transcript" is found throughout the specification and, for example, at p. 20, lines 13-18, wherein the instant application states, "[i]n a preferred embodiment of the invention, the cDNA sequence contains substantially non-coding sequences from either the 5'-end or the 3'-end of a transcript (e.g., produces less than 50% of a full length polypeptide encoded by a gene corresponding to the transcript and excludes repeat elements (e.g., *Alu* elements)." In view of the above, Applicant submits that one of skill in the art would recognize the art accepted usage of the phrase "corresponding to", when used in the context of nucleotides, as meaning a sequence of nucleotides that encodes, or is identical to a particular sequence.

Utility

Applicant submits that the invention as claimed clearly meets the legal requirements for utility under 35 U.S.C. § 101, "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."

According to the Guidelines for Examination of Applications for Compliance with the Utility Requirement (Section 2107 of the Manual of Patent Examining Procedure), the legal requirements for utility under 35 U.S.C. 101 are a well-established utility. "An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible...If

the Applicant has asserted that the claimed invention is useful **for any particular practical purpose** (i.e., it has a "specific and substantial utility") and the assertion would be **considered credible by a person of ordinary skill in the art**, do not impose a rejection based on lack of utility...A claimed invention must have a specific and substantial utility. This requirement excludes "throw-away," "insubstantial," or "nonspecific" utilities, such as the use of a complex invention as landfill, as a way of satisfying the utility requirement of 35 U.S.C. 101."

Applicant submits that the specification clearly discloses that the claimed invention is useful for numerous **"particular practical purposes"** (recited below) and a person of ordinary skill in the art would consider these uses **"credible."**

As discussed in Applicant's response after final rejection, filed on February 10, 2003, and as asserted herein, the claimed arrays of claims 1-13 are useful for: **1)** defining a pattern of gene expression representative of an entire cell, tissue or organism enabling an expression profile to be created for that cell, tissue or organism in both healthy and pathological states (see p.1 and 8); **2)** determining the expression profile of a previously unknown or uncharacterized gene or the expression profile of a known gene. (see p. 7 and 8); **3)**creating expression profiles of two or more genes and identifying interactions between genes (see p. 8); **4)** assessing the biological relevance of a previously unknown or uncharacterized gene (p. 8, lines 9-11); **5)** monitoring effects of a particular drug or set of drugs on gene expression; **6)** creating an expression profile for a given pathology; and **7)** determining the biological relevance of a previously unknown or uncharacterized gene

In view of all of the above, Applicant submits that the invention as claimed clearly meets the legal requirements for utility under 35 U.S.C. § 101.

Novelty

In response to the Examiner's suggestion, during the February 27, 2003 Examiner interview, that the pending claims of the instant application may not be novel in view of U.S. Patents 6,416,951, 6,312,901, 6,303,301 and 6,057,100, Applicant submits the following.

Applicant submits that for a determination of anticipation to be proper, the prior art reference must disclose each and every limitation of the claim. *Atlas Powder Company et al. v. IRECO, Incorporated et al.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999).

U.S. 6,416,951

U.S. 6,416,951 relates to methods and reagents for screening for functional antisense agents. At column 1, lines 36-53, U.S. 6,416,951 states, "Accordingly, the present invention provides a method for identifying a functional antisense agent, which method comprises hybridising an RNA with an oligonucleotide probe and measuring in real time the kinetics of hybridisation, wherein the kinetics are measured by either hybridising in the presence of an intercalation dye and recording a change in the spectroscopic properties of the dye as hybridising proceeds, or incorporating a label in either the RNA or the probe, attaching the non-labelled RNA or non-labelled probe to a solid support, generating an evanescent wave in the proximity of the non-labelled RNA or non-labelled probe and recording the increase in a signal generated by interaction of the evanescent wave with the label, as hybridisation proceeds, and wherein the **oligonucleotide probe comprises an array of oligonucleotides, each oligonucleotide in the array having a common length of 4 to 8 nucleotides, all possible base sequences of that length being represented in the array**." (Emphasis added)

U.S. 6,416,951 does not teach a nucleic acid member from 10 nucleotides to less than 1000 nucleotides, as claimed in claims 1 and 2 of the instant application.

U.S. 6,312,901

U.S. 6,312,901 relates to cleavable signal elements for quantitative and qualitative assay devices and methods. At column 5, lines 22-39, U.S. 6,312,901 states, "Each cleavable signal element comprises a cleavable spacer having a substrate-attaching end, a signal-responsive end, and a cleavage site intermediate the substrate-attaching end and the signal-responsive end. The cleavable signal element further includes a signal responsive moiety attached to the cleavable spacer at its signal responsive end. A **first side member** adapted to bind a first site on a chosen analyte, and a **second side member** adapted to bind a second site of the same analyte, are **present on the signal element**. The first and second side members confer analyte specificity

upon the cleavable signal element. The first side member is attached to the cleavable spacer intermediate said signal responsive end and said cleavage site, and the second side member is attached to the cleavable spacer intermediate said cleavage site and said substrate attaching end." (Emphasis added)

U.S. 6,312,901 also teaches at column 32, lines 60-61, "[i]n a preferred embodiment, the side members are oligonucleotides."

At column 34, lines 14-17, U.S. 6,312,901 states, "[w]hen trimers or tetramers are used to build oligonucleotides, two printing cycles allow one to create an array of all possible oligos from 6-mers to 8-mers."

U.S. 6,312,901 does not teach a nucleic acid member "from 10 nucleotides to less than 1000 nucleotides", as claimed in claims 1 and 2 of the instant application.

U.S. 6,303,301

U.S. 6, 303,301 relates to methods, compositions and apparatus for mapping the regulatory relationship among genes by massive parallel monitoring of gene expression. At column 10, lines 48-57, U.S. 6,303,301 states, "Preferred high density arrays for gene function identification and genetic network mapping comprise greater than about 100...oligonucleotide probes...The oligonucleotide probes range from about 5 to about 50 or about 500 nucleotides, more preferably from about 10 to about 40 nucleotide and most preferably from about 15 to about 40 nucleotides in length."

U.S. 6,303,301 does not teach either "an array comprising a plurality of nucleic acid members, each member having a unique position and stably associated with a solid substrate, **wherein each nucleic acid member comprises a sequence of nucleotides corresponding to a non-coding region of a 3'-end of an mRNA transcript**, and wherein each of said nucleic acid members is from 10 nucleotides to less than 600 nucleotides", as claimed in claim 1 of the instant application or, "an array comprising a plurality of nucleic acid members, each member having a unique position and stably associated with a solid substrate, **wherein each nucleic acid**

member comprises a sequence of nucleotides corresponding to a non-coding region of a 5' end of an mRNA transcript, and wherein each of said nucleic acid members is from 10 nucleotides to less than 1000 nucleotides", as claimed in claim 2 of the instant application. (Emphasis added)

U.S. 6,057,100

U.S. 6,057,100 relates to oligonucleotide arrays comprising a solid support of a plurality of different oligonucleotide pools arranged in a distinct linear row to form an immobilized oligonucleotide stripe, wherein the length of each stripe is greater than its width. At column 4, lines 7, U.S. 6,057,100 states, "The length of the oligonucleotide, i.e. the number of nucleotides, can vary widely, as will be appreciated by those in the art. Generally, oligonucleotides of at least 6 to 8 bases are preferred, with oligonucleotides ranging from about 10 to 500 being preferred, with from about 20 to 200 being particularly preferred, and 40 to 100 being especially preferred."

Applicant submits that U.S. 6,057,100 does not teach either "an array comprising a plurality of nucleic acid members, each member having a unique position and stably associated with a solid substrate, wherein each nucleic acid member comprises a sequence of nucleotides corresponding to a non-coding region of a 3'-end of an mRNA transcript, and wherein each of said nucleic acid members is from 10 nucleotides to less than 600 nucleotides", as claimed in claim 1 of the instant application, or, "an array comprising a plurality of nucleic acid members, each member having a unique position and stably associated with a solid substrate, wherein each nucleic acid member comprises a sequence of nucleotides corresponding to a non-coding region of a 5' end of an mRNA transcript, and wherein each of said nucleic acid members is from 10 nucleotides to less than 1000 nucleotides", as claimed in claim 2 of the instant application.

In view of the above, Applicant submits that claims 1-13 are novel over U.S. Patents 6,416,951, 6,312,901, 6,303,301 and 6,057,100.

CONCLUSION

In view of all of the above, and in view of the remarks presented in Applicant's response to the final Office Action, filed on February 10, 2003, Applicant submits that all claims are allowable as written and respectfully request favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

Respectfully submitted,

Date: March 10, 2003

Kathleen M. Williams
Reg. No. 34,380
PALMER AND DODGE, LLP
Customer No.: 27495
111 Huntington Avenue
Boston, MA 02199
Phone: (617) 239-0451
FAX: (617) 227-4420

MARKED UP CLAIMS

1. (Amended) An array comprising a plurality of nucleic acid members, each member having a unique position and stably associated with a solid substrate, wherein each nucleic acid member comprises a [non-coding] sequence of nucleotides corresponding to a non-coding region of [present in] a 3'-end of an mRNA transcript, and wherein each of said nucleic acid members is from 10 nucleotides to less than 600 nucleotides.

2. (Amended) An array comprising a plurality of nucleic acid members, each member having a unique position and stably associated with a solid substrate, wherein each nucleic acid member comprises a [non-coding] sequence of nucleotides corresponding to a non-coding region of [present in] a 5' end of an mRNA transcript, and wherein each of said nucleic acid members is from 10 nucleotides to less than 1000 nucleotides.

PENDING CLAIMS (3/03)

1. (Amended) An array comprising a plurality of nucleic acid members, each member having a unique position and stably associated with a solid substrate, wherein each nucleic acid member comprises a sequence of nucleotides corresponding to a non-coding region of a 3' end of an mRNA transcript, and wherein each of said nucleic acid members is from 10 nucleotides to less than 600 nucleotides.

2. (Amended) An array comprising a plurality of nucleic acid members, each member having a unique position and stably associated with a solid substrate, wherein each nucleic acid member comprises a sequence of nucleotides corresponding to a non-coding region of a 5' end of an mRNA transcript, and wherein each of said nucleic acid members is from 10 nucleotides to less than 1000 nucleotides.

3. The array of claim 1 or 2, wherein said noncoding sequence is at least 20 nucleotides in length.

4. The array of claim 1 or 2, wherein each said nucleic acid member comprises substantially noncoding sequences.

5. The array of claim 1, wherein said nucleic acid members comprise human sequences.

6. The array of claim 5, wherein at least one position on said array comprises a control position comprising a substance selected from the group consisting of: a buffer, a cDNA encoded by a housekeeping gene, a plant gene sequence, and a vector sequence.

7. The array of claim 1 or 2, wherein said array comprises from 1000 to 10,000 positions.

9. The array of claim 5, wherein said nucleic acid members comprise sequences expressed in at least two different tissues.

10. The array of claim 1 or 2, wherein said nucleic acid members comprise sequences expressed in a healthy tissue.

11. The array of claim 1 or 2, wherein said nucleic acid members comprise sequences expressed in a diseased tissue.

12. The array of claim 1 or 2, wherein said nucleic acid members comprise sequences expressed in a tissue which has been exposed to a drug.

13. The array of claim 1 or 2 wherein said nucleic acid members do not comprise repeat sequences.